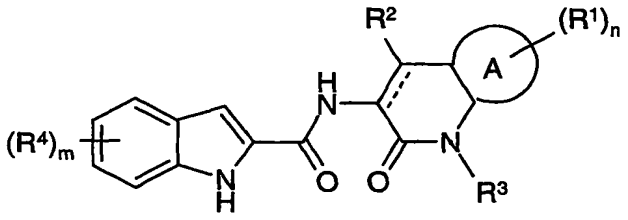
Claims

1. A compound of formula (1):



(1)

wherein:

⎓ is a single or double bond;

A is phenylene or heteroarylene;

m is 0, 1 or 2;

n is 0, 1 or 2;

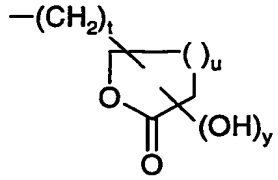
R^1 is independently selected from halo, nitro, cyano, hydroxy, carboxy, carbamoyl, *N*-C_{1-4}alkylcarbamoyl, *N*,*N*-(C_{1-4}alkyl)$_2$carbamoyl, sulphamoyl, *N*-C_{1-4}alkylsulphamoyl, *N*,*N*-(C_{1-4}alkyl)$_2$sulphamoyl, -S(O)$_b$$C_{1-4}$alkyl (wherein b is 0,1,or 2), C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, hydroxyC_{1-4}alkyl, fluoromethyl, difluoromethyl, trifluoromethyl and trifluoromethoxy;

or, when n is 2, the two R^1 groups, together with the carbon atoms of A to which they are attached, may form a 4 to 7 membered ring, optionally containing 1 or 2 heteroatoms independently selected from O, S and N, and optionally being substituted by one or two methyl groups;

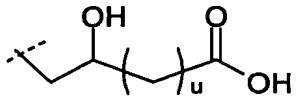
R^4 is independently selected from hydrogen, halo, nitro, cyano, hydroxy, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, carboxy, carbamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy and C_{1-4}alkanoyl;

R^2 is hydrogen, hydroxy or carboxy;

R^3 is selected from hydrogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkanoyl, carbamoyl, C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, aryl, heterocyclyl, C_{1-4}alkyl (optionally substituted by 1 or 2 R^8 groups), and groups of the formulae B and B':



(B)



(B')

wherein y is 0 or 1, t is 0, 1, 2 or 3 and u is 1 or 2; provided that the hydroxy group is not a substituent on the ring carbon adjacent to the ring oxygen;

R^8 is independently selected from hydroxy, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, C_{3-7}cycloalkyl, C_{1-4}alkanoyl, C_{1-4}alkoxy, C_{1-4}alkylS(O)$_b$- (wherein b is 0, 1 or 2), C_{3-6}cycloalkylS(O)$_b$- (wherein b is 0, 1 or 2), arylS(O)$_b$- (wherein b is 0, 1 or 2), heterocyclylS(O)$_b$- (wherein b is 0, 1 or 2), benzylS(O)$_b$- (wherein b is 0, 1 or 2), -N(OH)CHO, -C(=N-OH)NH_2, -C(=N-OH)NHC_{1-4}alkyl, -C(=N-OH)N(C_{1-4}alkyl)$_2$, -C(=N-OH)NHC_{3-6}cycloalkyl, -C(=N-OH)N(C_{3-6}cycloalkyl)$_2$, -COCOOR^9, -C(O)N(R^9)(R^{10}), -NHC(O)R^9, -C(O)NHSO$_2$(C_{1-4}alkyl), -NHSO$_2$R^9, (R^9)(R^{10})NSO$_2$-, -COCH$_2$OR^{11}, (R^9)(R^{10})N- and -COOR^9;

R^9 and R^{10} are independently selected from hydrogen, hydroxy, C_{1-4}alkyl (optionally substituted by 1 or 2 R^{13}), C_{3-7}cycloalkyl (optionally substituted by 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, trihalo(C_{1-4})alkyl, aryl, heterocyclyl and heterocyclyl(C_{1-4}alkyl); or R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring is optionally substituted on carbon by 1 or 2 substituents independently selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl, C_{1-4}alkoxy and heterocyclyl; or the ring may be optionally substituted on two adjacent carbons by –O-CH$_2$-O- to form a cyclic acetal wherein one or both of the hydrogens of the -O-CH$_2$-O- group may be replaced by a methyl;

R^{13} is selected from hydroxy, halo, trihalomethyl and C_{1-4}alkoxy;

R^{11} is independently selected from hydrogen, C_{1-4}alkyl and hydroxyC_{1-4}alkyl;

or a pharmaceutically acceptable salt or pro-drug thereof.

2. A compound of the formula (1) as claimed in claim 1, wherein

R^3 is selected from hydrogen, hydroxy, C_{1-4}alkoxy, C_{1-4}alkanoyl, carbamoyl, C_{3-7}cycloalkyl (optionally substituted with 1 or 2 hydroxy groups, cyano(C_{1-4})alkyl, phenyl, morpholino,

morpholinyl, piperidino, piperidyl, pyridyl, pyranyl, pyrrolyl, imidazolyl, thiazolyl, thienyl, thiadiazolyl, piperazinyl, isothiazolidinyl, 1,3,4-triazolyl, tetrazolyl, pyrrolidinyl, thiomorpholino, pyrrolinyl, homopiperazinyl, 3,5-dioxapiperidinyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrazolyl, pyrazolinyl, isoxazolyl, 4-oxopydridyl, 2-oxopyrrolidyl, 4-oxothiazolidyl, furyl, thienyl, oxazolyl, 1,3,4-oxadiazolyl, and 1,2,4-oxadiazolyl, tetrahydrothiopyranyl, 1-oxotetrahydrothiopyranyl, 1,1-dioxotetrahydrothiopyranyl and C_{1-4}alkyl (optionally substituted by 1 or 2 R^8 groups);

R^9 and R^{10} are independently selected from hydrogen, hydroxy, C_{1-4}alkyl (optionally substituted by 1 or 2 R^{13} groups), C_{3-7}cycloalkyl (optionally substituted by 1 or 2 hydroxy groups), cyano(C_{1-4})alkyl, trihalo C_{1-4}alkyl, aryl, heterocyclyl and heterocyclyl(C_{1-4}alkyl); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring is optionally substituted on carbon by 1 or 2 substituents selected from oxo, hydroxy, carboxy, halo, nitro, cyano, carbonyl and C_{1-4}alkoxy, or the ring may be optionally substituted on two adjacent carbons by $-O-CH_2-O-$ to form a cyclic acetal wherein one or both of the hydrogens of the $-O-CH_2-O-$ group may be replaced by a methyl;

R^8 is independently selected from hydroxy, C_{1-4}alkoxyC_{1-4}alkoxy, hydroxyC_{1-4}alkoxy, 5- and 6-membered cyclic acetals and mono- and di-methyl derivatives thereof, aryl, heterocyclyl, C_{3-7}cycloalkyl, C_{1-4}alkanoyl, C_{1-4}alkoxy, C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1 or 2), C_{3-6}cycloalkyl$S(O)_b$- (wherein b is 0, 1 or 2), aryl$S(O)_b$- (wherein b is 0, 1 or 2), heterocyclyl$S(O)_b$- (wherein b is 0, 1 or 2), benzyl$S(O)_b$- (wherein b is 0, 1 or 2), -N(OH)CHO, -C(=N-OH)NH_2, -C(=N-OH)NHC_{1-4}alkyl, -C(=N-OH)N(C_{1-4}alkyl)$_2$, -C(=N-OH)NHC_{3-6}cycloalkyl, -C(=N-OH)N(C_{3-6}cycloalkyl)$_2$, -COCOOR^9, -C(O)N(R^9)(R^{10}), -NHC(O)R^9, -C(O)NHSO_2(C_{1-4}alkyl), -NHSO_2R^9, (R^9)(R^{10})NSO_2-, -COCH_2OR^{11}, (R^9)(R^{10})N- and -COOR^9;

R^{13} is selected from hydroxy, halo, trifluoromethyl and C_{1-4}alkoxy;

R^{11} is selected from hydrogen, C_{1-4}alkyl and hydroxyC_{1-4}alkyl;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

3. A compound of the formula (1) as claimed in claim 1 or claim 2 wherein:

R^3 is selected from cyanoC_{1-4}alkyl and C_{1-4}alkyl (optionally substituted by 1 or 2 of R^8 groups);

R^8 is independently selected from hydroxy, phenyl, 2,2-dimethyl-1,3-dioxolan-4-yl; 2,2-dimethyl-1,3-dioxan-4-yl; 2,2-dimethyl-1,3-dioxan-5-yl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, triazolyl, tetrazolyl, imidazolyl, pyrrolidinyl, piperidyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiopyranyl and tetrahydrothienyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1 or 2), -C(O)N(R^9)(R^{10}), -COOR^9 , -C(O)NHSO_2Me, -C(=N-OH)NH_2 , -C(=N-OH)NHC_{1-4}alkyl, -C(=N-OH)N(C_{1-4}alkyl)$_2$ and –NHSO_2R^9;

R^9 and R^{10} are independently selected from hydrogen, hydroxy, C_{1-4}alkyl optionally substituted with R^{13} (wherein R^{13} is C_{1-4}alkoxy or hydroxy); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring where the ring may be optionally substituted on carbon by 1 or 2 hydroxy groups or carboxy groups), or the ring may be optionally substituted on two adjacent carbons by –O-CH_2-O- to form a cyclic acetal wherein one or both of the hydrogens of the –O-CH_2-O- group may be replaced by a methyl;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

4. A compound of the formula (1) as claimed in any preceding claim, wherein:

R^3 is selected from cyanoC_{1-4}alkyl and C_{1-4}alkyl (optionally substituted by 1 or 2 R^8 groups);

R^8 is independently selected from hydroxy, 2,2-dimethyl-1,3-dioxolan-4-yl, 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, tetrazolyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkyl$S(O)_b$- (wherein b is 0, 1 or 2), -C(O)N(R^9)(R^{10}), -COOR^9 , -C(O)NHSO_2Me, -C(=N-OH)NH_2;

R^9 and R^{10} are independently selected from hydrogen, hydroxy, C_{1-4}alkyl optionally substituted with R^{13} (wherein R^{13} is C_{1-4}alkoxy or hydroxy); or

R^9 and R^{10} together with the nitrogen to which they are attached form a 4- to 6-membered ring selected from piperidine, 4-hydroxy piperidine, pyrrolidine, 3,4-dihydroxypyrrolidine and the dimethylacetal of 3,4-dihydroxypyrrolidine;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

5. A compound of the formula (1) as claimed in any preceding claim, wherein:

m is 1 and R^4 is chlorine;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

6. A compound of the formula (1) as claimed in any preceding claim, wherein:

A is phenylene;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

7. A compound of the formula (1) as claimed in any one of claims 1 to 5, wherein:

A is heteroarylene;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

8. A compound of the formula (1) as claimed in any preceding claim, wherein:

 is a single bond;

or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof.

9. A compound of the formula (1) as claimed in claim 1, which is any one of:

5-chloro-*N*-[1-(methoxycarbonylmethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

N-[1-(carboxymethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-5-chloroindole-2-carboxamide;

5-chloro-*N*-(2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-[{2-oxo-1-[2-oxo-2-(pyridin-2-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylthio)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylsulphinyl)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[2-(methylsulphonyl)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(1,3,4-thiadiazol-2-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-methylpyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(pyridin-3-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-methyl-1,3,4-thiadiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-cyano-1*H*-pyrazol-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-methyl-1,3-thiazol-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-chloropyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-hydroxypyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(pyridin-2-ylmethyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(pyridin-4-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-methyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1,3-dimethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(pyrazin-2-ylmethyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-fluoropyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(2-hydroxypyrimidin-4-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(pyrimidin-4-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-ethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-oxo-2-[(5-oxo-4,5-dihydro-1*H*-pyrazol-3-yl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(4-hydroxypyrimidin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-methylpyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(6-chloropyridazin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1*H*-imidazol-2-ylmethyl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(1-methyl-1*H*-pyrazol-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-{2-oxo-1-[2-oxo-2-(2*H*-tetrazol-5-ylamino)ethyl]-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(3-ethyl-1*H*-pyrazol-5-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(5-fluoropyridin-2-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

N-(1-{2-[(6-bromopyridin-3-yl)amino]-2-oxoethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-5-chloro-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(2-hydroxyethyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[(2,2-dimethyl-1,3-dioxan-5-yl)methyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[3-hydroxy-2-(hydroxymethyl)propyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(2,3-dihydroxypropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(3-hydroxy-2-oxopropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

5-chloro-*N*-{1-[(2*R*)-2,3-dihydroxypropyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-1*H*-indole-2-carboxamide;

5-chloro-*N*-(1-{2-[(methylsulfonyl)amino]ethyl}-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

N-{1-[2-(acetylamino)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-5-chloro-1*H*-indole-2-carboxamide;

5-chloro-*N*-(2-oxo-1-{2-[(trifluoroacetyl)amino]ethyl}-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*-indole-2-carboxamide;

5-chloro-*N*-[1-(3-hydroxypropyl)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide;

N-{1-[(2*Z*)-2-amino-2-(hydroxyimino)ethyl]-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl}-5-chloro-1*H*-indole-2-carboxamide;

5-chloro-*N*-(6-fluoro-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl)-1*H*- indole-2-carboxamide; and

5-chloro-*N*-[6-(methyloxy)-2-oxo-1,2,3,4-tetrahydroquinolin-3-yl]-1*H*-indole-2-carboxamide; or a pharmaceutically acceptable salt or an in-vivo hydrolysable ester thereof.

10. A pharmaceutical composition which comprises a compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9 in association with a pharmaceutically-acceptable diluent or carrier.

11. A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9, for use in a method of treatment of a warm-blooded animal such as man by therapy.

12. A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9, for use as a medicament.

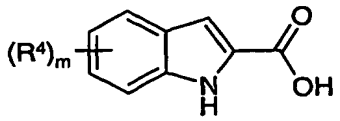
13. A compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9, for use as a medicament in the treatment of type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia or obesity in a warm-blooded animal such as man.

14. The use of a compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9, in the manufacture of a medicament for use in the treatment of type 2 diabetes, insulin resistance, syndrome X, hyperinsulinaemia, hyperglucagonaemia, cardiac ischaemia or obesity in a warm-blooded animal such as man.

15. The use of a compound of the formula (1), or a pharmaceutically acceptable salt or in-vivo hydrolysable ester thereof, as claimed in any one of claims 1 to 9, in the manufacture of a medicament for use in the treatment of type 2 diabetes in a warm-blooded animal such as man.

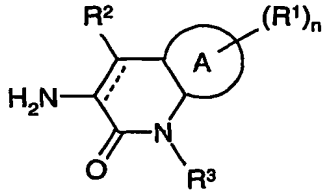
16. A process for the preparation of a compound of formula (1) as claimed in claim 1, which process comprises:

reacting an acid of the formula (2):



(2)

or an activated derivative thereof; with an amine of formula (3):



(3)

and thereafter if necessary:

i) converting a compound of the formula (1) into another compound of the formula (1);

ii) removing any protecting groups;

iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.